REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Response to Rejection of Claims 80-82 and 84-85 under 35 U.S.C. Section 112, first paragraph (new matter/ written description).

The claims are rejected on the basis that the limitations drawn to "various transdominant negative PLB genes" are "not disclosed on pages 10-11 of the Specification." (Action at page 2, center paragraph). The rejection is a new matter rejection.

However, the claims in question are fully supported by written description in the original specification; in particular, original claims 35-40 (see, e.g., In re Koller, 204 USPQ 702 (CCPA 1980) [original claims constitute their own description]; accord, In re Gardner, 177 USPQ 396 (CCPA 1973) and In re Wertheim, 191 USPQ 90 (CCPA 1976)). Therefore, Applicant respectfully submits that the rejection of claims 80-82 and 84-85 as being directed to new matter should be reconsidered and withdrawn.

The Action also indicates that a written description rejection from a prior action against the claims had not been fully addressed by Applicant's last response (of November 14, 2005) because the claims at issue had not been amended. Applicant respectfully disagrees.

The prior written description rejection in question contended that the claims exceeded their supported scope by extending to any method for gene therapy using a phospholamban molecule in the heart. Applicant responded by limiting the scope of the claims to the method exemplified in Example II of the Specification; i.e., enhancing the transduction efficiency of a gene therapy vector. To that end, Claim 70, from which each of claims 80-82 and 84-85 depend (through Claim 79), was amended to recite that the claimed method increased the efficiency of transduction by delivering a mutated PLB gene into the heart while the patient is in a state of hypothermia (see Amendment of November 14, 2005 at page 2, Claim 70). By dependency, these limitations were therefore introduced by amendment into claims 80-82, and 84-85 just as if each of the claims had been individually amended to add the new limitations.

For all the foregoing reasons, the amended claims are fully supported by the Specification as detailed in the November 14, 2005 Amendment at page 7. Reconsideration and withdrawal of all grounds of rejection based on "new matter" is therefore respectfully requested.

II. Response to Rejection of Claims 70-72 and 77-97 under 35 U.S.C. Section 112, first paragraph (enablement).

The present Office Action reiterates an assertion from a prior action that the claims are not enabled. In this respect, the Action identifies the claimed invention as: ". . . the treatment of any cardiac disease by administering any viral vector encoding PLB-S16E gene, wherein the viral vector is administered to the heart via any route of administration." (Action at page 6, last paragraph). However, Applicant respectfully submits that this is not an accurate characterization of the claims which, as of the Amendment of November 14, 2005, are directed to a method for enhancing the transduction efficiency of a gene that has been introduced into the heart for the purpose of treating cardiac disease by placing the subject into a state of hypothermia.

The Office Action is silent with respect to the hypothermia and transduction limitations of the claims, so Applicant assumes that their practice is considered to have been enabled. Further, Applicant notes that the Action concedes that "intra-coronary administration of an AAV-PBL (S16E) [molecule which] results in increased cardiac contractility and reduce the occurrence of interstitial fibrosis" is enabled. (Action at pages 6-7, bridging paragraph).

The enablement issue therefore appears to be based on the question of whether use of the invention to treat "any and all cardiac diseases" would require undue experimentation by one of ordinary skill in the art. Applicant respectfully disagrees.

Firstly, the end point presently claimed is not a therapeutic result, but is instead an increase in transduction efficiency of a set of genes. Efficacy of the genes in achieving a therapeutic result is therefore only marginally relevant, if at all, to the question of whether the invention *as claimed* is enabled. However, for purposes of advancing prosecution, Applicant addresses the therapeutic result question as follows.

In contending that one of ordinary skill would have difficulty treating cardiac disease, the Action states that "heart failure, cardiac contractility and relaxation, regulation of calcium handling in cardiomyocytes and regulation of calcium uptake into sarco-endoplasmic reticulum in calcium cells etc. each having considerably different etiologies."

The underlined portion of the foregoing passages appears to reflect a misunderstanding of the nature of heart disease. In particular, "cardiac contractility and relaxation, regulation of calcium handling in cardiomyocytes and regulation of calcium uptake into sarco-endoplasmic reticulum" are not disease conditions, and do not have etiologies. Rather, each is a normal function of heart muscle. Abnormalities in one or more of those functions can lead to (and are hallmarks of) heart failure. Conversely, suppressing physiologic phospholamban inhibition of SERCA2 activity enhances calcium uptake into the sarco-endoplasmic reticulum. Such uptake regulates cardiac myocyte contraction and relaxation. Enhancement of these functions had a therapeutic benefit in treatment of heart disease (see, e.g., review of the art in MacLennan and Kranias, *Nat.Rev.Mol.Cell Biol.*, 4: 566-577 (2003); submitted herewith).

The Specification enables use of the invention to these ends, in particular in the context of treating heart failure, the target condition recited in all pending claims (see Claim 1). The invention claimed is a method which enhances transduction efficiency of the mutant phospholamban molecule that is used to suppress physiologic phospholamban inhibition of SERCA2 activity. Practice of the invention to treat heart failure by improving cardiac contractility (and its corollary, relaxation) is demonstrated in an art-accepted model of human heart failure, the hamster animal model of paragraph 0011 and Examples 6 through 8 (paragraphs 0039 through 0043).

With the foregoing understanding of the invention as claimed and its clinical context, Applicant submits that enablement of the invention by the Specification is clear. Reconsideration and withdrawal of the rejection of Claims 70-72 and 77-97 is therefore respectfully requested.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date 6-13, 2006

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